

Amendment and Response

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Serial No.: 09/483,337

Confirmation No.: 8254

Filed: 14 January 2000

**For: COMPOSITIONS AND METHODS FOR NONENZYMATIC LIGATION OF OLIGONUCLEOTIDES AND
DETECTION OF GENETIC POLYMORPHISMS**

providing a mutant polymorphism oligonucleotide probe that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

wherein one oligonucleotide probe constitutes an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group and the other oligonucleotide probe constitutes a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when both probes are bound to the target polynucleotide, an end of the universal oligonucleotide probe is not directly adjacent to an end of the mutant polymorphism oligonucleotide probe so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target polynucleotide with the universal oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and the mutant polymorphism probe; and

detecting the presence of the autoligated oligonucleotide product.

45. **(Amended)** The method of claim 44 wherein at least one of the mutant polymorphism oligonucleotide probe and the universal oligonucleotide probe further comprises a detectable label.

50. **(Amended)** A method for detecting a genetic polymorphism in a target polynucleotide comprising:

providing a mutant polymorphism oligonucleotide probe of less than 7 nucleotides in length that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

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providing a wild-type polymorphism oligonucleotide probe that is complementary to a region on an analogous wild-type polynucleotide that is analogous to the region comprising the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

wherein either (i) the universal oligonucleotide probe constitutes an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group and both polymorphism oligonucleotide probes constitute downstream oligonucleotides comprising, as their 3' ends, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate; or (ii) both polymorphism oligonucleotide probes constitute upstream oligonucleotides comprising, as their 5' ends, a nucleoside comprising a 5' leaving group and the universal oligonucleotide probe constitutes a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when a universal probe and a polymorphism probe are bound to the target polynucleotide, an end of the universal oligonucleotide probe is substantially adjacent to an end of the polymorphism oligonucleotide probe so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target polynucleotide with the universal oligonucleotide probe, the wild-type polymorphism oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and either the mutant polymorphism oligonucleotide probe or the wild-type polymorphism oligonucleotide probe; and

detecting the presence of the autoligated oligonucleotide product.

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C² Cond
51. **(Amended)** The method of claim 50 wherein at least one of the mutant polymorphism oligonucleotide probe and the universal oligonucleotide probe further comprises a detectable label.

C³
57. **(Amended)** The method of claims 56 wherein at least one of the mutant polymorphism oligonucleotide probe and the universal oligonucleotide probe further comprises a detectable label.
